



Case report

Liver abscess caused by *Lawsonella clevelandensis* in a patient with rheumatoid arthritis: A case report and literature review



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ABSTRACT

Lawsonella clevelandensis is a recently described anaerobic and partially acid-fast bacterium within the order *Corynebacterineae*. It is a fastidious microorganism that has been identified as part of the oral microbiota and is rarely associated with human infections. We describe the case of a 70-year-old man with a history of rheumatoid arthritis that developed liver abscesses and pylephlebitis. Gram stain of purulent material obtained by percutaneous drainage of the hepatic collection revealed gram-positive bacilli that stained acid-fast by the Kinyoun method. The patient was initially treated with imipenem, moxifloxacin and clarithromycin for possible *Nocardia* and/or nontuberculous mycobacterial infection. Cultures failed to grow the organism seen on the stains, and broad-spectrum 16S rRNA PCR gene sequencing analysis identified it as *Lawsonella clevelandensis*. Treatment was de-escalated to amoxicillin/clavulanic acid. The hepatic abscesses resolved completely after 4 weeks of treatment.

There are only 8 documented cases of human infection caused by *Lawsonella clevelandensis* reported in the literature. Conventional microbiological methods do not reliably detect this bacterium, and the diagnosis relies on molecular methods. Excellent outcomes are obtained with a combined treatment approach that includes abscess drainage and prolonged antibiotic therapy.

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Introduction

Lawsonella clevelandensis is an anaerobic, partially acid-fast bacillus recently recognized as a human pathogen. It is difficult to isolate in conventional cultures, thus diagnosis relies on molecular techniques based on gene sequencing analysis [1]. Human infections are extremely rare. To our knowledge, there are only 8 cases of infection caused by this organism documented in the English literature. Abscesses in the abdominal cavity, breast, and spine have been described [2]. We present a case of *Lawsonella clevelandensis* liver abscess with pylephlebitis and review the existing literature.

Case description

A 70-year-old man was admitted to the hospital with two months of abdominal pain, fatigue, unintentional 40-pound weight loss, and one week of subjective fevers and shortness of breath. He described his abdominal pain as diffuse, non-radiating, and constant, without aggravating or relieving factors. His shortness of breath started a week prior to admission and progressed to being able to walk only a few steps. His past medical history was significant for rheumatoid arthritis, for which he was on treatment with methotrexate and adalimumab for 1 year. He also suffered of hypertension, hyperlipidemia, diverticulosis, and sleep apnea. Three months before onset of symptoms, the patient had an uneventful dental procedure. The patient was a retired marine who went to Vietnam in 1961 and stayed there for 13 months. He denied any sick contacts.

Upon admission, his temperature was 37.8 °C, pulse was 98 beats/min, respiratory rate was 14 breaths/min, and blood pressure was 87/53 mmHg. His abdominal exam revealed a distended and diffusely tender abdomen with guarding and normal bowel sounds. No hepatosplenomegaly was noted. Laboratory studies

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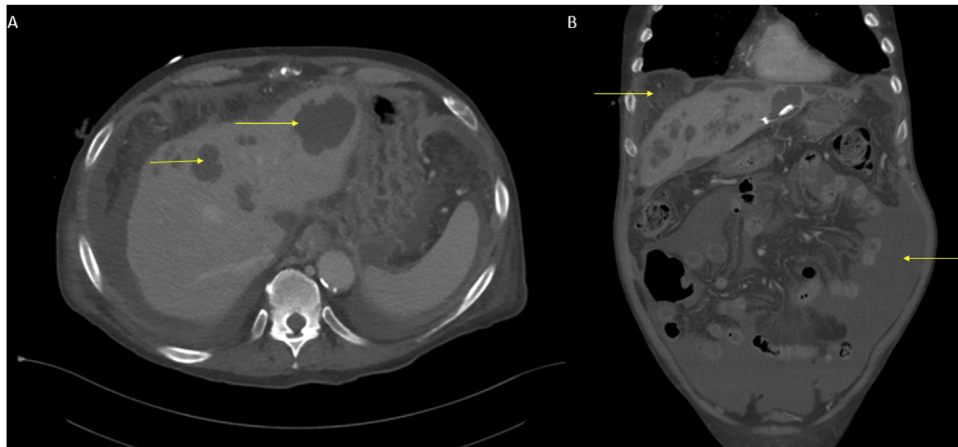


Fig. 1. Contrast CT scan showing numerous low-density lesions within the liver, likely representing hepatic abscesses (A) and abdominal/pelvic ascites probably due to venous congestion (B).

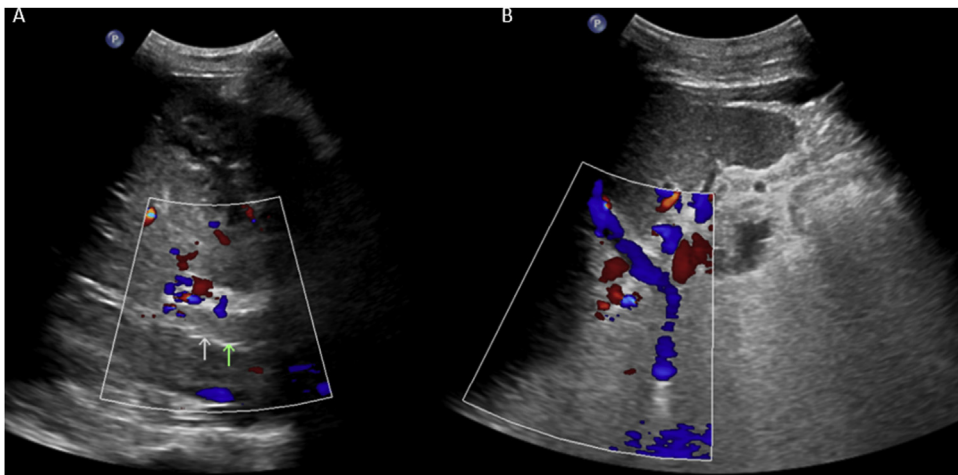


Fig. 2. Doppler ultrasound demonstrating portal vein (A) and splenic vein (B) thrombosis.

showed 19,300 leukocytes/uL with 91 % neutrophils, hemoglobin of 12.2 g/dL, platelet count of 245,000/uL, elevated transaminases (AST: 136 IU/L, ALT: 96 IU/L), mild hyperbilirubinemia (2.1 mg/dL), and elevated alkaline phosphatase (415 IU/L). His creatinine was 1.6 mg/dL, up from his baseline of 0.9 mg/dL one month prior. A computed tomography with contrast of the abdomen showed numerous low-density lesions within the liver (Fig. 1A). There was also thrombosis of the hepatic veins in the right lobe of the liver that extend to involve the entire portal vein and the central portion of the splenic vein, which was later confirmed by Doppler ultrasound (Fig. 2A,B). Other significant findings included cholelithiasis, ascites (Fig. 1B) and bowel wall edema involving the small bowel, cecum, ascending colon and transverse colon. A paracentesis was performed with removal of 2.3 liters of cloudy fluid. Analysis of ascitic fluid revealed albumin of 0.9 g/dL, total protein of 2.5 g/dL, and 1734 leukocytes/uL with 77 % of neutrophils. Approximately 55 mL of purulent material were obtained by percutaneous drainage of the hepatic collections, and a Jackson-Pratt (JP) drain was placed in right upper quadrant. Piperacillin/tazobactam, vancomycin, and metronidazole were administered empirically for a suspected polymicrobial liver abscess.

Microbiological studies of the liver drainage and ascitic fluid revealed beaded gram-positive rods, which also stained acid-fast on Kinyoun stain (Fig. 3), raising the concern for non-tuberculous

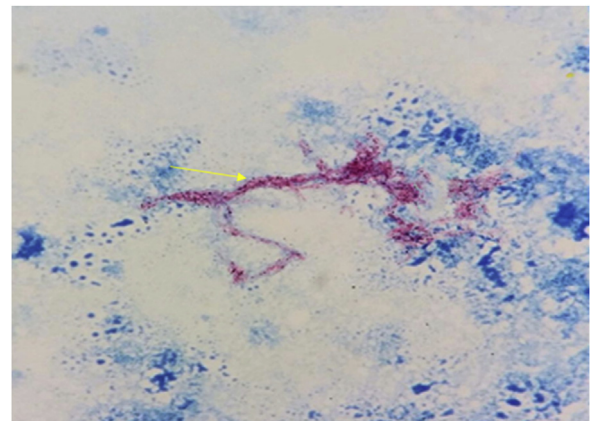


Fig. 3. Direct microscopy showing acid-fast bacilli by Kinyoun method (x200).

mycobacteria and *Nocardia*. Antimicrobial treatment was modified to imipenem, moxifloxacin, and clarithromycin. He remained afebrile and clinically stable and was discharged home on this antimicrobial regimen. One week later, the culture remained



Fig. 4. Contrast CT scan showing resolution of hepatic abscesses at 1-month follow-up.

negative, but 16S rRNA gene sequencing (752 bp) showed 100 % identity to *Lawsonella clevelandensis*. Antimicrobial therapy was de-escalated to oral amoxicillin/clavulanic acid 875 mg twice a day based on our literature review for similar cases. At one-month follow up, CT scan showed complete resolution of abscesses (Fig. 4). The JP drain was removed, and antimicrobial therapy was discontinued at that time. After 3-months of follow-up, there was no evidence of recurrent infection. The patient has been kept off immunosuppressants and has not developed any flares of his rheumatologic condition.

Discussion

Lawsonella clevelandensis is an anaerobic, partially acid fast-bacterium that belongs to the suborder *Corynebacterineae*. It was named *Lawsonella* to honor Paul A. Lawson (English microbiologist from University of Oklahoma), and *clevelandensis* after Cleveland, Ohio, the city of origin of the type strain. The presence of mycolic acids in its cell wall makes it structurally related to the aerobic actinomycetales [2]. This fastidious microorganism requires a prolonged incubation period and is sometimes confounded with other organisms (mainly *Nocardia* spp.) due to their morphologic similarities. The microbiologic identification of this organism relies on 16S rRNA gene sequencing most times [1]. Documented infections caused by *Lawsonella clevelandensis* are extremely rare, but it has been reported to cause abscesses in the abdominal cavity, breast, and spine in post-surgical and immunocompromised patients [2].

We searched MEDLINE via OVID and EMBASE via Scopus for the relevant Medical Subject Headings terms in English-language literature. The terms included in our search were “*Lawsonella*” and “*clevelandensis*”. We considered only those cases in whom the organism was identified as the cause of infection. We also reviewed the references of these reports for additional relevant literature. We found 8 case reports fitting our search criteria [3–7] (Table 1). The mean age of afflicted patients was 43.3 years, ranging from 2 to 81 years. The male to female ratio was 1:1. The majority of cases were described in USA and Canada (75 %), with only 2 cases reported from Europe (Portugal and United Kingdom). Five (63 %) patients presented certain degree of immunosuppression that included neoplastic conditions, rheumatologic diseases, and diabetes mellitus. In addition, two patients reported taking

Table 1
Summary of Cases Reported in the Literature for *Lawsonella clevelandensis* infection.

Ref	Age(y) sex	Country of origin	Underlying disease	Immunosuppressive medications	Infection	Procedure to control the infection	Antibiotic therapy	Outcome
[3]	65/M	Cleveland, Ohio, USA	Metastatic prostate cancer	Prednisone	Abscess in thoracic spine, osteomyelitis with hardware	Incision and drainage, partial hardware removal, debridement	VAN -> SAM -> MPM -> SXT -> AMC	Death
[3]	44/F	Winnipeg, Manitoba, Canada	Diabetes mellitus, liver steatosis, obesity	None	Breast abscess	Incision and drainage	VAN -> CLOXA -> AMC	Cure
[3]	23/F	Winnipeg, Manitoba, Canada	Diabetes mellitus, recurrent furunculosis	None	Breast abscess	Incision and drainage	CIP + MTZ -> SXT	Cure
[3]	81/M	New York, USA	Polymyalgia rheumatica, coronary artery disease, aortic stenosis	Prednisone	Liver abscess	Percutaneous aspiration, drain placement	LVX + MTZ + VAN + CLI + SXT -> CLI + SXT -> SXT	Cure
[4]	64/M	Ohio, USA	Neuroendocrine tumor s/p distal pancreatectomy and splenectomy, Diabetes mellitus, obesity	None	Intraabdominal abscess	Percutaneous drainage, catheter placement, exploratory laparotomy	CIP + MTZ -> VAN + MPM -> TGC -> ETP + SXT	Cure
[5]	29/F	Lisbon, Portugal	None	None	Breast abscess	Surgical drainage	SXT -> AMC	Cure
[6]	38/M	Maryland, USA	Ulcerative colitis s/p total proctocolectomy	None	Intraabdominal abscess	Laparoscopy and percutaneous drain placement	Broad spectrum antibiotics -> Antitubercular treatment -> AMC	Cure
[7]	2/F	Nottingham, United Kingdom	Beckwith-Weidemann syndrome, infected dermoid cyst	None	Spinal subdural empyema	Surgical drainage	CXM + MTZ -> AMC -> CXM -> LZD	Cure
Present report	70/M	Miami, USA	Rheumatoid arthritis, cirrhosis, diverticulosis	Methotrexate, adalimumab	Liver abscess	Percutaneous drainage and drain placement	TZP + VAN + MTZ -> IPM + MXF + CLR -> AMC	Cure

Ref, reference; y, years; M, male; F, female; s/p, status post; VAN, vancomycin; SAM, ampicillin/sulbactam; MPM, meropenem; SXT, trimethoprim-sulfamethoxazole; AMC, amoxicillin/clavulanic acid; CLOXA, cloxacillin; CIP, ciprofloxacin; MTZ, metronidazole; LVX, levofloxacin; CLI, clindamycin; TGC, tigecycline; ETP, ertapenem; CXM, cefuroxime; LZD, linezolid; TZP, piperacillin/tazobactam; IPM, imipenem; MXF, moxifloxacin; CLR, clarithromycin.

prednisone. Our patient's clinical characteristics were similar to the ones described in the literature. He was immunocompromised due to his history of rheumatoid arthritis and was on chronic treatment with methotrexate and adalimumab.

Harrington et al. reported a patient with polymyalgia rheumatica receiving prednisone who developed multiple liver abscesses. No history of prior surgical intervention was reported in this patient [3]. This case is very similar to the one described in the present report, since both manifested as liver abscesses and occurred in immunocompromised patients with no surgical history. Two (25 %) cases presented with intra-abdominal abscesses after abdominal surgery [4,6]. One of them was a patient who underwent distal pancreatectomy and splenectomy for resection of a pancreatic neuroendocrine tumor and developed a peri-pancreatic abscess one-month post-surgery [4]. The other case had a recent history of total proctocolectomy with ileal pouch-anal anastomosis and developed an intra-abdominal abscess in the right lower quadrant [6]. Three of the eight cases of *Lawsonella clevelandensis* infection presented as breast abscesses [3,5]. Two of these patients were diabetic, and one of them did not have any relevant medical history. The presentation was subacute or chronic in all of them, with a slow progression over the course of 3 weeks to 3 months. Other infections documented in the literature included a case of thoracic spine abscess with osteomyelitis that developed as a complication of surgical spinal stabilization, and a case of spinal subdural empyema resulting from an infected spinal dermoid cyst [3,7]. The patient with osteomyelitis reported a history of immunosuppression due to metastatic prostate cancer and chronic treatment with prednisone [3].

The environmental niche for *Lawsonella clevelandensis* is still unknown; however, recent studies have isolated *Lawsonella* in the oral human microbiome [8]. It is uncertain if this organism is part of the skin flora, but this possibility has been suggested by cases of breast abscess and post-surgical infections which originated most likely from the skin [3–6]. In some cases, the relationship with abdominal surgeries has raised the possibility that this microorganism is part of the normal gut flora [4]. In the present case, we postulate that the organism reached the liver by hematogenous spread from an oral source. Our patient's history of a prior dental procedure may support this hypothesis. However, another potential source is the bowel, which is plausible due to our patient's history of diverticulosis. Although no signs of diverticular abscesses or intestinal perforation were noted on imaging, our patient could have developed microperforations in the large bowel that led to portal vein pyemia and resulted in seeding of the liver and development of pylephlebitis. Our patient's ascitic fluid, consistent with secondary peritonitis (low serum-ascites albumin gradient (SAAG) and high total protein in ascitic fluid) makes bowel microperforations highly possible in this setting. Although there are no reported cases of *Lawsonella clevelandensis* infection related to the use of tumor necrosis factor blockers (adalimumab), previous reports suggest a relationship between this organism and an immunosuppressed state [3]. We believe that the use of immunomodulators for the treatment of the rheumatoid arthritis in this case played an important role on the pathophysiology of the infection.

The morphologic appearance of *Lawsonella* makes this microorganism easily confounded with other related strains such as *Nocardia* and *Actinomyces*. In the case described by Chudy-Onwugaje et al., as well as in our case, the infection was attributed initially to a mycobacterial infection given the presence of acid-fast bacilli on smear, and in our case to the fact that the patient was on a tumor necrosis factor inhibitor (adalimumab). In both cases, the patients were eventually switched to amoxicillin/clavulanic acid after identification of *Lawsonella* by molecular techniques [6].

Drainage of infected collections has been crucial to successfully treat all the cases reported. In our patient, percutaneous aspiration

and drain placement aided in the complete resolution of liver abscess. There is no standardized antibiotic therapy for this organism, and the selection of antimicrobials is entirely based on case reports. Given its poor growth in liquid media, antibiotic susceptibility testing has never been accomplished. The most common antibiotics used for definitive treatment have been amoxicillin/clavulanic acid (5 patients) and trimethoprim/sulfamethoxazole (3 patients) [3–7]. In most cases, treatment was initiated with broad-spectrum antibiotics and then de-escalated based on gram-stain results, growth in anaerobic cultures, or gene sequencing analysis.

Regarding the duration of treatment, most authors favor prolonged antibiotic therapy, ranging from 2 to 17 months [3–7]. Our patient received 6 weeks of antibiotics that included 2 weeks of broad-spectrum antibiotics and 4 weeks of monotherapy with oral amoxicillin/clavulanic acid. Completion of treatment was reached when there was complete radiological resolution of the liver collections and the JP drain was removed.

The outcomes of patients with *Lawsonella clevelandensis* infection are generally favorable, and most of them achieve cure after abscess drainage and prolonged antibiotic therapy. Only one fatal case has occurred in a patient who developed abscess of the spine and osteomyelitis with hardware involvement; however, the patient's death was attributed to complications of his underlying condition (metastatic prostate cancer) and not to the infection itself [3]. Based on these reports, we hypothesize that *Lawsonella clevelandensis* is a low-virulent species that becomes pathogenic in immunocompromised hosts and in patients with recent surgical interventions.

Conclusions

Lawsonella clevelandensis is a novel anaerobic, partially acid-fast bacterium that morphologically can mimic other organisms such as mycobacteria and actinomycetes. The diagnosis is challenging due to the limitations of conventional methods for isolating this microorganism. Our case highlights the importance of obtaining molecular identification of unidentified organisms causing culture-negative collections, especially in immunocompromised patients. The treatment is not standardized; however, we have obtained excellent outcomes with abscess drainage and prolonged antibiotic therapy with amoxicillin/clavulanic acid.

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Credit author statement

Jose A. Gonzales Zamora participated in the conceptualization of the article and wrote the manuscript. Zachary Henry, Maria Romero, Paola Lichtenberger, Gio Baracco, and Gordon Dickinson were involved in direct patient care. Paola Lichtenberger and Gio Baracco reviewed and edited the manuscript. All the authors reviewed and approved the final version of the article.

Declaration of Competing Interest

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